52. (new) A diagnostic kit comprising a protein-binding diagnostically effective substance according to claim 49, pharmaceutically acceptable auxiliary, substance, a carrier or a diluent.

53. (new) A method for detecting cancer diseases, auto immune diseases, acute or chronic inflammatory diseases and diseases which are caused by viruses or microorganisms, or for detecting the carrier molecule and its distribution in the body comprising utilizing the kit of claim 52.

54. (new) A process for producing an injectable medicament preparation, which comprises a diagnostically effective substance which is dissolved in an injectable carrier liquid, wherein the diagnostically effective substance is a compound which comprises a diagnostic agent and at least one protein-binding molecular residue.

55. (new) A process according to Claim 35, wherein the diagnostic agent and the protein-binding molecular residue are linked by a spacer.

56. (new) A process according to Claim 35, wherein the bond between the diagnostic agent and the protein-binding molecular residue or the spacer is not cleavable.

57. (new) A process according to Claim 37, wherein the diagnostic agent and the protein-binding molecular residue are linked to each other by an amide bond.

REMARKS

Reconsideration of this application, as amended, is respectfully requested.

The Examiner has rejected to claims 20, 30, 31 and 35 under 35 U.S.C. § 112, second paragraph, because the term "spacer" as allegedly vague. Claims 20 and 35 were rejected under the same statute because the expression "protein binding molecular residue" is allegedly vague. Applicants respectfully traverse. The term "spacer" is defined on page 7, line 20 of the corresponding WO publication and on page 8, lines 9-12 of the English translation. Likewise, the protein binding molecule is defined as on page 8, lines 1-5 of the WO publication and page 8, lines 26-31 of the translation. Preferred "spacers" and "protein binding molecule" are found in claims 25 and 26. Accordingly, withdrawal of the 35 U.S.C. § 112, second paragraph rejections is respectfully requested.

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Claims 20-38 were rejected under §102(b) as allegedly anticipated by Trouet. Applicants respectfully traverse.

Trouet discloses daunorubicin conjugated to succinylated serum albumin, which is totally different than the claimed invention. In this context, please note the general structure of the medicaments obtained according to the invention on page 4, line 17. As can be clearly gathered therefrom, these active compounds just do not contain the protein, like serum albumin, which Trouet discloses. It is clear from the description of the present invention that the very gist of the invention is to use an injectable medicament preparation which, after injection, is capable of covalently binding to an endogenous protein, however, does not yet contain the protein, contrary to the compound proposed by Trouet. Surprisingly, preparations of the invention, after injection, react with particular proteins present in the body and are then transported by these proteins to the site of action in the organism. If the site of action are tumor cells, which are characterized by containing proteinases which either are not found in healthy cells or in considerably smaller amounts, the compounds bound to the protein are split there and become effective selectively only at the site of action. As a result, a considerably smaller amount of active agent is necessary to achieve the same effect as in the case of the previously known formulations of the same active agent.

These facts are further explained in the introduction of the present application. In particular, it is stated therein that it is known to couple derivatized cytostatic agents to a protein such as albumin (cf. WO, page 2, 1st paragraph and paragraph bridging pages 1 and 2 of the English translation, respectively). Trouet does not teach anything besides what was known already from the prior art according to DE 196 36 869 and PCT/DE97/02000. The drawbacks of such substances are discussed at page 2, lines 17-22.

None of the cited references provide a description that would lead the skilled person to the understanding that it would be possible to form such protein and albumin conjugates, respectively, only in vivo by injecting a reactive intermediate. It was also not known what percentage of the injected compounds can be expected actually to react with proteins, nor could it be foreseen, whether the compound would bind just to those proteins which enable transport of the active substance to the desired site of action, i.e. a tumor cell.

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The skilled artisan knows that a major portion of the body's proteins can be found also on tissue surfaces, so one would have had the concern that the injected active agent derivative is fixed onto the tissue and remains ineffective. Therefore, it was extremely surprising to find that, by means of the injectable reactive agent derivatives of the invention superior action can be achieved compared to known forms of the active agent. In this context, please note especially Example 3, wherein the doxorubicin derivative used according to the invention (DOXO HYD) is compared with doxorubicin itself and shows clearly superior action compared with doxorubicin, of, in particular, the Figures on page 28 of the English text.

From the above, it can be said that superior action is achieved with the presently claimed invention compared to the results of free active agents. The advantages of the invention compared with substances as described by Trouet are pointed out on page 2, lines 17-22 of the English specification It could not be expected from the cited reference that these advantages could be achieved according to the presently claimed invention.

In view of the foregoing, allowance is respectfully requested.

Applicant believes no fee is due with this response. However, if a fee is due, please charge Deposit Account No. 50-0624, under Order No. NY-HUBR 1198-US from which the undersigned is authorized to draw.

Dated: March 2, 2004

Respectfully submitted,

By _____

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